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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,804	08/03/2006	Mallen Huang	1503-1063	6727

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
07/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/551,804	HUANG, MALLEN	
	Examiner	Art Unit	
	SHANON A. FOLEY	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 14-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 14-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/19/05 and 09/07/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 44-69, and 73-74 in the reply filed on 07/20/2009 is acknowledged. The traversal is on the ground(s) that there is a technical relationship among claims 44, 63, 69, and 70. The technical relationship is based on the special technical features of the nucleotide vaccine composition i.e. being a mixture of nucleotide sequence encoding an antigen and APCs modified for expression of at least one of an immune response modulating molecule and a cell-survival modulating molecule. Applicant points out that the Office Action discusses that PCT Rule 13 permits unity for the combination of a product, a first process of making the product and a first method of using the product. Applicant also discuss that Annex B of the Administrative Instructions does not disclose that unity is permitted only for the combination of product, a first process of making the product and a first method of using the product, thus the interpretation of only permitting a single method of use has been made in the Office Action without an support from the Administrative Instructions. Lastly, Applicants argue that part 1b of the Annex B of the Administrative Instructions specifies that special technical features are those features that define the contribution which each of the inventions considered as a whole, makes over the prior art and determination of lack of unity is art-based and requires the citation of the special technical feature.

Applicant's traversal has been fully considered, but is found unpersuasive because: the method for determining unity of invention under PCT Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:

(A) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product; or
(B) In addition to an independent claim for a given process, an independent claim for an apparatus or means specifically designed for carrying out the said process; or
(C) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product and an independent claim for an apparatus or means specifically designed for carrying out the said process..

For Example, the inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: PCT Rule 13 permits unity for the following combination: a product, a first process of making the product and a first method of using the product. Any subsequent method for making and using the product lacks unity of invention with the first group. In the instant case, the first method of using the product claimed is found in instant claim 69, where an immune response is induced upon administration of the instant vaccine. The second method of using the product, i.e. Group II, is drawn to a method of treating or preventing a disease upon administration of the instant vaccine, see claim 70.

Accordingly, any subsequent patentably distinct invention lacks unity with the first group, see 37 CFR § 1.476 (d).

Applicant's election of the species natural-interferon producing cells, CD40 ligand, apoptosis inducing gene, and plasmid in the reply filed on 07/20/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant states that the species relating to immune response modulating molecule relates to the

immune response modulating molecule defined in claim 44, and 54-55 whereas claims 58-61 relate to an immune response modulating nucleotide sequence which is a different species. The Examiner acknowledges Applicant's election of the immune regulating molecule CD40 ligand as pertaining to claims 44, 54, and 55.

The requirement is still deemed proper and is therefore made FINAL.

Claims 70-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/20/2009.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see paragraph [0137]. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44-69, 73 and 74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims require a nucleotide vaccine comprising a mixture of a nucleotide sequence encoding an antigen and antigen-presenting cells "modified for expression of" an immune response modulating molecule and a "cell-survival modulating molecule". While there is ample discussion provided for modifying an antigen-presenting cell to express a CD40L, see Figure 6 and paragraphs [0142, 0143, 0147, 0163, 0165, 0171, ect.], there is no teaching provided for modifying an antigen presenting cell to express any "cell-survival modulating molecule", as recited, and therefore required, by the claims. There is no support provided for the scope of possible cell-survival modulating molecules encompassed by the instant claims. There is no description provided for the genus of possible cell-survival modulating molecules, or whether these molecules are intended to be chemical compounds, nucleic acids, peptides or proteins. There is an insufficient description regarding the structural relationship that would provide a nexus between the instant genus of cell-survival modulating molecules claimed and the function they are required to possess.

In instant claim 56, the cell-survival modulating molecule is required to be (the elected species) "an apoptosis inducing gene". In paragraph [0019] of the instant specification, there is a teaching that the instant APCs are genetically modified to express, among other things, anti-apoptosis agents or apoptosis-inducing agents, but there is no mention of specific apoptosis agents within the scope of the claim.

There are a myriad of possible molecules in the art that may modulate the survival of a cell in the mitochodrial pathway and the death receptor pathways, see the overview of Jin et al. (Cancer Biology and Therapy.2005; 4 (2): e50-e74). Jin et al. discuss molecules that trigger apoptosis via death receptor pathways, including TNF, Fas and TRAIL. However, Jin et al. also

discuss decoy receptors that evade apoptosis, see "extrinsic apoptotic pathways" bridging pages e54-e55. In the mitochondrial pathway, there are also pro-apoptotic agents and anti-apoptotic agents, see "intrinsic apoptotic pathways" bridging pages e59-e61.

Given the plethora of members and agents involved in receptor-mediated and intrinsic cellular pathways in apoptosis and immortalization, the skilled artisan would be unable to sufficiently identify common structural elements required in any "cell-survival modulating molecule" or genetic material to induce apoptosis, as instantly required. The instant disclosure does not reasonably convey possession for modifying an antigen presenting cell to express any "cell-survival modulating molecule", possession of the broad genus of possible cell-survival modulating molecules or possession of a genus of possible apoptosis inducing genes claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 44-47, 57, 60, 69, 73 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Kontani et al. (Cancer Gene Therapy. 2002; 9: 330-337, provided in the IDS).

Kontani et al. anticipate a nucleotide vaccine composition comprising a mixture (top of first column on page 332) of a plasmid encoding an antigen, MUC1 (see "plasmid DNA" on page 331) and a subclass of antigen-presenting dendritic cells (see Preparation of DCs on page 331). Kontani et al. anticipate producing an immune response by administering the vaccine composition, see the paragraph bridging pages 331-332.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 48-56, 58, 59, 61, 63-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kontani et al. *supra*, Kikuchi et al. (Blood. 2000; 96 (1): 91-99, provided in the IDS) and Krug et al. (European Journal of Immunology. 2001; 31: 3026-3037).

See the teachings of Kontani et al. above. Kontani et al. do not teach or suggest modifying a plasmacytoid dendritic cell to express CD40L or adding an unmethylated CpG sequence to a nucleic acid sequence encoding the tumor antigen of Kontani et al.

Kikuchi et al. teach modifying dendritic cells to express CD40L, see "cytokines" on page 92.

One of ordinary skill in the art at the time the invention was made would have been motivated to modify dendritic cells to express CD40L to enhance T-cell activation and anti-tumor antigen presentation, see Figure 8 on page 96, the paragraph bridging the columns on page 97 and "Dendritic cell-based cancer immunotherapy" bridging pages 97-98.

Neither Kikuchi et al. nor Kontani et al. teach or suggest modifying a plasmacytoid-type dendritic cell or adding an unmethylated CpG sequence to a nucleic acid sequence encoding the tumor antigen.

However, Krug et al. teach toll-like receptors on plasmacytoid dendritic cells are required for recognition of CpG motifs, see Krug et al. also specifically demonstrate that synergistic

activation of plasmacytoid dendritic cells, stimulating the production of IL-12, IFN-α and bioactive IL-12 p70, see section 2.4 and Figures 5 and 9.

One of ordinary skill in the art at the time the invention was made would have been motivated to modify the plasmacytoid dendritic cells of Krug et al. to express CD40L and to add the CpG motif to the nucleotide antigen vaccine of Kontani et al. to induce a synergistic activation of PDCs for production of IL-12. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for inducing synergistic activation of PDCs in the presence of CD40L and a CpG nucleotide motif since Krug et al. specifically teach that toll-like receptors present on PDCs are responsible for recognition of CpG motifs and that synergistic activation of PDC's is accomplished through simultaneous presence of CD40L and CpG nucleic acids. One of ordinary skill in the art at the time the invention was made would have had further reasonable expectation of success for modifying PDC's to express CD40L since Kikuchi et al. demonstrate successful expression of CD40L on dendritic cells.

Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kontani et al., Kikuchi et al. and Krug et al. as applied to claims 44-61, 63-68, 69, 73 and 74 above, and further in view of Fritz et al. (WO 02/069900).

See the teachings of Kontani et al., Kikuchi et al. and Krug et al. above. None of the references teach or suggest SEQ ID NO: 5.

However, Fritz et al. teach a sequence comprising instant SEQ ID NO: 5, see the sequence alignment provided below:

Query Match 100.0%; Score 47; DB 1; Length 21;
Best Local Similarity 100.0%;

Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 AFHGDAEAL 9
||||||||||
Db 5 AFHGDAEAL 13

One of ordinary skill in the art at the time the invention was made would have been motivated to use the fusion protein sequence of Fritz et al. with a reasonable expectation of success in the vaccine composition of Kontani et al., Kukichi et al. and Krug et al. to treat cancer, see claim 29 of Fritz et al.

Allowable Subject Matter

The prior art does not teach or suggest SEQ ID NOs 3 or 4.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANON A. FOLEY whose telephone number is (571)272-0898. The examiner can normally be reached on flex, generally M-F 7AM - 3 PM, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shanon A. Foley/
Primary Examiner
Art Unit 1619